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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,530	04/07/2004	Dennis Benjamin	PPI-144	8326

959 7590 12/21/2007

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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
12/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,530	BENJAMIN ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-18 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-17* is/are rejected.

7)☒ Claim(s) *18,26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5 have been canceled. Any objections and/or rejections from previous office actions that have not been reiterated in this office action are obviated.

The examiner suggested the allowance of claims 26 (independent) and 7-10 (dependent) to applicant's representative (Debbie Nagle) via a telephone call. The applicants rejected this suggestion.

Claim Objections

1. Claim 26 is objected to because of the following informalities: it contains two method steps labeled (c) whereas one should be labeled as step (e). Appropriate correction is required.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 6-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for ovalicin, fumagillin, fumagillol, and fumagillin analogs does not reasonably provide enablement for all "test compounds that are inhibitors of MetAP-2". The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to utilize the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

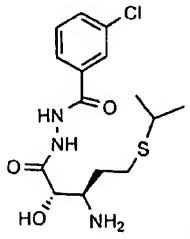
1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

1. The nature of the invention, state of the prior art, relative skill of those in the art, and the predictability of the art

The claimed invention relates to a method for determining the extent of inactivation of MetAP-2 by administering a "test compound that is an inhibitor of MetAP-2", which encompasses any inhibitor of MetAP-2. There are various inhibitors of MetAP-2 that are known in the art, such as A-357300 (Wang et al. Cancer Res. 2003, 63, 7861-7869). The inhibitor A-357300 has a completely different structure (see

below) than those listed above and there is no clear indication in the specification of the use of other inhibitors of MetAP-2 than those stated above for the instant invention.



A-357300

2. The breadth of the claims

The claims are very broad and inclusive of "test compound that is an inhibitor of MetAP-2" generally, which includes any inhibitor of MetAP-2. Clearly, the methods are only used which inhibitors of MetAP-2, such as ovalicin, fumagillin, fumagillol, and fumagillin analogs

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction for ascertaining, *a priori*, any other inhibitors of MetAP-2 that may be utilized commensurate in scope with the instant invention. There is not indication as to what appropriate structural characteristics are necessary for the "test compound that is an inhibitor of MetAP-2" to be useful for the method of the instant invention.

4. The quantity of experimentation necessary

The lack of adequate guidance from the specification or prior art with regard to determining suitable "test compounds that are inhibitors of MetAP-2" except for those listed above. Applicants fail to provide the guidance and information required to

ascertain which "test compounds that are inhibitors of MetAP-2" will be usable with the instant invention.

3. Claims 6-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has not described in a reasonable generic manner to show support for any test compound that may have the activity of being an inhibitor of MetAP-2. Applicant has not described a correlation of between the structure and function for the test compounds of the instant claims and also the assays for determining the test compound of the instant claims are not described. Thus, the assays for determining the compounds do not provide a description of the structural/physical or chemical features required for the test compounds of the instant claims. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 6-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to which test compound or biological target to use for the method of measuring the ability of a test compound to inactivate a biological target in the instant claims 6-13. The administration of different compound will vary with regards to dose or the biological target of interest. The recitation of a "test compound which is an inhibitor of a biological target" does not impart any physical or structural characteristics necessary for the test compounds of the instant claims to indicate the scope of the claimed compounds.

Response to Arguments

5. Applicant's arguments filed 11/16/07 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 6-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Turk et al. (*Chem. Biol.* **1999**, *6*, 823-833) in view of Soker et al. (US 2005/0112063A1) as stated in the office action mailed 5/18/07. The modified rejection was necessitated by the amendment to the claims.

8. Applicant asserts that there is no teaching or suggestion in Turk et al. to administer a test compound to a subject or removing a plurality of biological samples from the subject.

9. The examiner concedes that Turk et al. does not teach of the administration of the fumagillin analog to a subject or removing biological samples from the subject.

10. Applicant asserts that Soker et al. fails to teach or suggest that the excised liver may be, or is used to determine the amount of free anti-angiogenic compound in the single or plurality of biological samples removed from a subject.

11. The reference of Soker et al. teaches of the method of measuring the ability of a test compound to inhibit a biological target via the administration of an antiangiogenic compound, such as a polymer conjugated TNP-470 to a subject in vitro or in vivo and assessing the bioeffectiveness of the compound via the removal of a sample (i.e. blood) from the subject. Also, Soker et al. teaches that the excision of the liver shows inhibition of liver regeneration upon treatment with TNP-470 which is an antiangiogenic compound. It would be obvious to one skilled in the art that a sample or multiple samples (i.e. blood) taken from a patient can be used to measure the ability of the test compound to inhibit a biological target. Also, it would be obvious that the measure of the inhibition of regeneration of a liver sample taken from a subject is a direct correlation

of the inhibition of angiogenesis as TNP-470 is an antiangiogenic compound. Therefore a plurality of samples (i.e. blood, liver) can be removed from the subject to measure the ability of a test compound to inhibit a biological target.

12. Claims 6-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (*Proc. Natl. Acad. Sci.* **1998**, *95*, 15183-15188) in view of Soker et al. (US 2005/0112063A1) as stated in the office action mailed 5/18/07. The modified rejection was necessitated by the amendment to the claims.

13. Applicant asserts that Griffiths et al. fails to teach of an in vivo assay or removing a plurality of biological samples from the subject.

14. The examiner concedes that Griffiths et al. does not teach of the administration of the fumagillin analog to a subject or removing biological samples from the subject.

15. Applicant asserts that Soker et al. fails to teach or suggest that the excised liver may be, or is used to determine the amount of free anti-angiogenic compound in the single or plurality of biological samples removed from a subject.

16. The reference of Soker et al. teaches of the method of measuring the ability of a test compound to inhibit a biological target via the administration of an antiangiogenic compound, such as a polymer conjugated TNP-470 to a subject in vitro or in vivo and assessing the bioeffectiveness of the compound via the removal of a sample (i.e. blood) from the subject. Also, Soker et al. teaches that the excision of the liver shows inhibition of liver regeneration upon treatment with TNP-470 which is an antiangiogenic compound. It would be obvious to one skilled in the art that a sample or multiple

samples (i.e. blood) taken from a patient can be used to measure the ability of the test compound to inhibit a biological target. Also, it would be obvious that the measure of the inhibition of regeneration of a liver sample taken from a subject is a direct correlation of the inhibition of angiogenesis as TNP-470 is an antiangiogenic compound. Therefore a plurality of samples (i.e. blood, liver) can be removed from the subject to measure the ability of a test compound to inhibit a biological target.

Conclusion

No claims are allowed at this time. Claim 18 is objected to for depending on a rejected claim and claim 26 is free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
December 7, 2007

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER